DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDAs 21-427/S-018, 18-936/S-081/S-082, 20-101/S-037, 21-235/S-009, 21-520/S-013/S-014

Eli Lilly and Company
Attention: Dr. Ann R. Sakai, Ph.D.
Associate Director, Regulatory Affairs
Lilly Corporate Center
Indianapolis, Indiana 46285

Dear Dr. Sakai:

We acknowledge receipt of your supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cymbalta (Duloxetine HCl) capsules (NDA 21-427) dated May 31, 2007, Prozac and Sarafem (fluoxetine HCl) capsules (NDA 18-936) dated June 1,and 4, 2007, Prozac (fluoxetine HCl) oral solution (NDA 20-101) dated June 1, 2007, Prozac (fluoxetine HCl) delayed release capsules (NDA 21-235) dated June 1, 2007, and Symbyax (olanzapine/fluoxetine HCl) capsules (NDA 21-520) dated January 10, 2007 (S-013) & June 15, 2007 (S-014).

We additionally refer to an Agency letter dated May 1, 2007, requesting revisions to your prescriber labeling and Medication Guide based upon the December 13, 2006 meeting of the Psychopharmacologic Drugs and Advisory Committee.

Reference is also made to an e-mail communication from the Agency dated June 21, 2007, requesting additional revisions to the labeling, and your e-mail dated June 22, 2007 accepting these changes.

Supplemental application 21-520/S-013, submitted under "Changes Being Effected" provides for the following revisions to labeling:

- Multiple revisions throughout the labeling to incorporate safety changes made to the Prozac (fluoxetine HCl) and Zyprexa (olanzapine) labelings.

Supplemental applications 21-427/S-018, 18-936/S-081/S-082, 20-101/S-037, 21-235/S-009, 21-520/S-014, submitted under "Changes Being Effected" provide for the following revisions to labeling:

1. Revisions to the Black Box entitled **Suicidality and Antidepressant Drugs** at the beginning of the prescriber labeling.
2. Revisions to the **WARNINGS-Clinical Worsening and Suicide Risk** section.
3. Revisions to the **PRECAUTIONS-Information for Patients** section.
4. Revisions to the **MEDICATION GUIDE**.

We have completed our review of these applications. These applications are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

However, we note that the enclosed labeling also includes changes proposed in your pending "Changes Being Effected" supplemental applications (NDA 21-427/017, 21-520/004), submitted May 17, 2007 & February 22, 2007, respectively. Please note that this approval does not apply to the changes proposed in the pending supplemental applications. We are currently evaluating the pending applications and will comment on the changes in a separate action letter.

Within 21 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission "SPL for approved supplements 21-427/S-018, 18-936/S-081,S-082, 20-101/S-037, 21-235/S-009, 21-520/S-013 & S-014."

We expect that the revised labeling would be available on your website within 10 days of receipt of this letter and that it would accompany any newly shipped product in a reasonable amount of time. Drug product already in distribution with currently approved labeling may remain in distribution.

Failure to make these changes within the specified period of time could make your product misbranded under 21 USC 321(n) and 352(a).

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

In addition, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed the revised product labeling and has determined that it contains significant new risk information relating to your drug product. We are hereby requesting that all promotional materials for your drug product that include representations about your drug product be revised to include the new risk information immediately. These revisions should include prominent disclosure of the important new information described in the **WARNINGS** and **PRECAUTIONS** sections that appear in the revised package labeling. Please submit a written response to this request 14 days from the date of this letter stating whether you intend to comply with this request, to the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications by facsimile at (301)796-9878 or at 5901-B Ammendale Road, Beltsville, MD 20705.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Renmeet Grewal, Pharm. D., Regulatory Project Manager, at (301) 796-1080 or Bill Bender, Regulatory Project Manager, at 301-796-2145.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Thomas Laughren
8/2/2007 10:52:25 AM